Efficiency of HIV-1 Pooled Viral Load Testing to Reduce the Cost of Monitoring ART in a Resource-limited Setting: Rural Malawi

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Background

- Routine HIV-1 viral load (VL) monitoring is important during the follow-up of people on ART to detect:
  - treatment failure early
  - virological failure

- Two obstacles to the roll-out of routine VL monitoring:
  1. High cost (25$-70$ per test)
  2. Logistical difficulties
     - Sample collection - phlebotomy
     - Sample transport - within six hours

- New strategies are needed to overcome these obstacles.
Rationale

1. Pooling strategies using plasma specimens have shown to:
   a) Reduce costs (by 40 to 60%)
   b) Maintain accuracy (NPV > 97%)

2. Using finger prick dried blood spots (FP DBS) as a sample type:
   a) Acceptable alternative for plasma
   b) More practical than using plasma:
      - FP means no need for phlebotomy
      - DBS means no need for fast sample transport system

This study combined the use of a pooling strategy with the use of FP DBS in a district laboratory.
Study objectives

a) Determine the efficiency and cost savings of pooled VL testing on DBS samples.

a) Determine the accuracy of pooled DBS testing as compared to individual plasma VL testing.
Methodology

Eligible patient (>6 months on ART and >18 years old)

- Finger-prick blood
  - 5 spot filter paper (FP-DBS)
    - Individual
    - Pooled

- EDTA venous blood
  - 5 spot filter paper (EDTA-DBS)
    - Individual
    - Pooled
  - Blood centrifuged (Plasma)
    - Individual
    - Pooled

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Pooling: how does it work? (1)

- Pool = a combination of several samples mixed together
- Pool size = the number of samples per pool
  - In this study pool size = 5

![Diagram showing pooling process]

Sample 1: 500 µL
Sample 2: 500 µL
Sample 3: 500 µL
Sample 4: 500 µL
Sample 5: 500 µL
Pool: 500 µL

Viral load testing

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Pooling: how does it work? (2)

- Two clinical thresholds for virological failure:

  1. Pooled VL result < threshold => no further testing
  2. Pooled VL result > threshold => further testing

<table>
<thead>
<tr>
<th>Individual</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000 cps/mL</td>
<td>200 cps/mL</td>
</tr>
<tr>
<td>5,000 cps/mL</td>
<td>1,000 cps/mL</td>
</tr>
</tbody>
</table>

- What to do with pooled viral load results?
  1. Pooled VL result < threshold => no further testing
  2. Pooled VL result > threshold => further testing
## Results (1)

### Demographics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>350 individuals</td>
</tr>
<tr>
<td>Gender</td>
<td>70.5% female</td>
</tr>
<tr>
<td>Median Age (Interquartile range)</td>
<td>38 years (20 – 46 years)</td>
</tr>
<tr>
<td>Median time on ART (Interquartile range)</td>
<td>37 months (18 – 65 months)</td>
</tr>
<tr>
<td>Reason for viral load testing</td>
<td>Routine (83.7%)</td>
</tr>
<tr>
<td>Suspected (16.3%)</td>
<td></td>
</tr>
<tr>
<td>Viral load detectability (&gt; 1,000 cps/mL)</td>
<td>8.0%</td>
</tr>
<tr>
<td>Viral load detectability (&gt; 5,000 cps/mL)</td>
<td>6.6%</td>
</tr>
</tbody>
</table>
Results (2)

- **Efficiency** - proportion of tests saved:

<table>
<thead>
<tr>
<th>Sample type</th>
<th>1,000 cps/mL</th>
<th>5,000 cps/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>44.3 %</td>
<td>48.6 %</td>
</tr>
<tr>
<td>FP DBS</td>
<td>28.6 %</td>
<td>51.4 %</td>
</tr>
<tr>
<td>EDTA DBS</td>
<td>32.9 %</td>
<td>51.4 %</td>
</tr>
</tbody>
</table>

- **Accuracy** at 1,000 cps/mL:

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Sensitivity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>95.0 %</td>
<td>99.5 %</td>
</tr>
<tr>
<td>FP DBS</td>
<td>90.0 %</td>
<td>99.0 %</td>
</tr>
<tr>
<td>EDTA DBS</td>
<td>95.0 %</td>
<td>99.5 %</td>
</tr>
</tbody>
</table>
Results (3)

Efficiency expressed as cost savings:

- Example of Thyolo District
  - Population: 620,000
  - HIV prevalence: 14.5%
  - # VL tests needed/year: 23,000
  - Price per VL test: $24

- Total cost/year = 23,000 x $24 = $552,000
  - Efficiency at 1,000 cps/mL = 28.6% => $157,800 saved
  - Efficiency at 5,000 cps/mL = 51.4% => $283,700 saved
Conclusions

- Pooling methods in combination with the use of FP DBS as a sample type for VL testing can importantly reduce costs while maintaining accuracy.

- In combination with the logistical advantages of FP DBS, these cost-savings can presumably enable the scale-up of viral load testing.

- Future studies will have to look into the effect of pooling methods on turn-around-time.
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